

a) modifying the genome of mammalian cells comprising a wild-type target locus by introducing a construct comprising two regions of sequences that are homologous to the 5' and 3' flanking sequences of said wild-type target locus;

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b) identifying cells containing said deletion by selecting cells containing a selectable marker present in said construct; and

c) recovering mammalian cell comprising said deletion.

3. (Amended) The method of claim 2 wherein said target locus is an HPRT locus.

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4. (Amended) The method of claim 2 wherein said target locus is an MHC Class I locus.

5. (Amended) The method of claim 2 wherein said target locus is an MHC Class II locus.

6. (Amended) The method of claim 2 wherein said target locus is an immunoglobulin locus.

7. (Amended) The method of claim 2 wherein said mammalian cell is selected from the group consisting of the islets of Langerhans, adrenal medulla cells, osteoblasts, osteoclasts, epithelial cells, endothelial cells, B lymphocytes, T lymphocytes, neurons, glial cells, ganglion cells, retinal cells, keratinocytes, embryonic stem (ES) cells, liver cells, bone marrow cells, and muscle cells.